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(FILE 'HOME' ENTERED AT 08:53:16 ON 23 JAN 2001)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 08:53:24 ON 23 JAN 2001

L1	77699	S	P53
L2	3535870	S	CANCER OR NEOPL? OR CARCINOMA OR TUMOR OR TUMOUR
L3	7249462	S	PROGNOSTICAT? OR DIAGNOS? OR SCREEN? OR DEVELOPMENT
L4	611200	S	DOMAIN OR CONSERVED
L5	568188	S	MUTATION
L6	492	S	L1 AND L2 AND L3 AND L4 AND L5
L7	213	DUP REM	L6 (279 DUPLICATES REMOVED)
L8	676434	S	CLASSIF?
L9	8	S	L8 AND L6
L10	5	DUP REM	L9 (3 DUPLICATES REMOVED)
L11	851960	S	STAGE
L12	35	S	L11 AND L6
L13	17	DUP REM	L12 (18 DUPLICATES REMOVED)
L14	869343	S	PROGRESS?
L15	248407	S	PROGRESSION
L16	21	S	L10 OR L13
L17	21	DUP REM	L16 (0 DUPLICATES REMOVED)

L17 ANSWER 1 OF 21 MEDLINE
ACCESSION NUMBER: 2000400106 MEDLINE
DOCUMENT NUMBER: 20383195
TITLE: Genetic alternations of p73 are infrequent but may occur in early ***stage*** hepatocellular ***carcinoma*** .
AUTHOR: Peng C Y; Tsai S L; Yeh C T; Hung S P; Chen M F; Chen T C; Chu C M; Liaw Y F
CORPORATE SOURCE: Liver Research Unit, Chang Gung Memorial Hospital, Chang Gung University, Taipei, Taiwan.
SOURCE: ANTICANCER RESEARCH, (2000 May-Jun) 20 (3A) 1487-92. Journal code: 59L. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY WEEK: 20001003
AB p73, a structural homologue of the ***tumor*** suppressor gene, ***p53*** , has recently been identified and mapped to chromosome 1p36, where genomic loss of heterozygosity (LOH) often occurs in human hepatocellular ***carcinoma*** (HCC). To determine whether p73 is involved in the ***development*** of HCC and whether there is an inverse correlation between the mutations of p73 and ***p53*** , we examined 22 paired tumors/noncancerous liver tissues for allelic expression, LOH and ***mutation*** of p73 and for ***mutation*** of ***p53*** . p73 was biallelically expressed in noncancerous liver tissues and in 7 out of the 8 informative tumors. One ***tumor*** tissue expressed only a single allele. LOH of p73 was found in 2 out of the 11 (18%) informative cases. A ***tumor*** -specific five-nucleotide deletion ***mutation*** causing a reading frameshift/early truncation of p73 DNA-binding ***domain*** was found, in which case no concomitant ***mutation*** in the DNA-binding ***domain*** of

p53 was identified. Nine out of the 22 cases (41%) contained ***tumor*** -specific mutations in the DNA-binding ***domain*** of ***p53*** . Two of the three cases with p73 genetic alternations had a ***tumor*** size of less than 2 centimeters. These results suggest that p73 is a biallelically expressed gene in the liver and that allelic loss and ***mutation*** of p73 is infrequent and may occur early in HCC. p73 is unlikely to be the putative ***tumor*** suppressor gene located at chromosome 1p36 in HCC.

L17 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare ***screening*** and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	
GB 1998-12099	19980606
GB 1998-13291	19980620
GB 1998-13611	19980624
GB 1998-13835	19980627
GB 1998-14110	19980701
GB 1998-14580	19980707
GB 1998-15438	19980716
GB 1998-15574	19980718
GB 1998-15576	19980718
GB 1998-16085	19980724
GB 1998-16086	19980724
GB 1998-16921	19980805
GB 1998-17097	19980807
GB 1998-17200	19980808
GB 1998-17632	19980814
GB 1998-17943	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response.

In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, ***development*** , progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L17 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare ***screening*** and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
PRIORITY APPLN. INFO.:			GB 1998-12098	19980606
			GB 1998-28289	19981223
			GB 1998-16086	19980724
			GB 1998-16921	19980805
			GB 1998-17097	19980807

GB 1998-17200 19980808
GB 1998-17632 19980814
GB 1998-17943 19980819
WO 1999-GB1779 19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response.

In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, ***development*** , progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L17 ANSWER 4 OF 21 MEDLINE
ACCESSION NUMBER: 1999356072 MEDLINE
DOCUMENT NUMBER: 99356072
TITLE: ***P53*** genotyping - an effective concept for molecular testing of head and neck ***cancer*** ?.
AUTHOR: Dahse R; Fiedler W; von Eggeling F; Schimmel B; Koscielny S; Beleites E; Claussen U; Ernst G
CORPORATE SOURCE: Institute of Human Genetics and Anthropology, Jena, Germany.
SOURCE: Int J Mol Med, (1999 Sep) 4 (3) 279-83.
Journal code: C8H. ISSN: 1107-3756.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY WEEK: 19991104

AB ***P53*** mutations are currently recognized as the most common genetic alteration in human tumors. The purpose of our study was to evaluate the significance and reliability of ***p53*** genotyping in head and neck ***cancer*** as a possible marker permitting the prediction of ***tumor*** behavior and clinical outcome. ***P53*** genotyping in our study refers to highly sensitive molecular ***screening*** in order to detect structural alterations in the nucleic acid sequence of the gene. Exons 2-11 and adjacent intronic regions were ***screened*** for mutations by direct genomic sequencing or by bi-directional dideoxyfingerprinting in 66 primary tumors of the larynx, pharynx and oral cavity. Alterations in the <hot spot region> of the ***p53*** gene were detected in 36% (24 of 66) of the analyzed tumors, no ***mutation*** was found in our cohort outside exons 5-8. The frequency of ***p53*** ***mutation*** had no correlation to the ***tumor*** ***stage*** or ***tumor*** site. The recurrence rate

in patients with a ***p53*** alteration was not significantly higher compared to patients without a ***p53*** ***mutation*** in their primary tumors. Summarizing the results of our study only limited reliability of ***p53*** genotyping as an effective concept for molecular testing of head and neck ***cancer*** was found.

L17 ANSWER 5 OF 21 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:83659 BIOSIS
DOCUMENT NUMBER: PREV199900083659
TITLE: ***p53*** mutations and expression in ovarian cancers: Correlation with overall survival.
AUTHOR(S): Wen, Wen-Hsiang; Reles, Angela; Runnebaum, Ingo B.; Sullivan-Halley, Jane; Bernstein, Leslie; Jones, Lovell A.; Felix, Juan C.; Kreienberg, Rolf; El-Naggar, Adel; Press, Michael F. (1)
CORPORATE SOURCE: (1) Norris Topping Tower Room 5410A, 1441 Eastlake Ave., U.S.C. Sch. Med., Los Angeles, CA 90033 USA
SOURCE: International Journal of Gynecological Pathology, (Jan., 1999) Vol. 18, No. 1, pp. 29-41.
ISSN: 0277-1691.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The ***p53*** gene is altered in apprx50% of all human malignancies. ***p53*** overexpression, identified by immunohistochemistry, and ***p53*** mutations, identified by single-strand conformational polymorphism (SSCP) and DNA sequencing, have been described in ovarian cancers. ***p53*** overexpression has been correlated with poor outcome for women with ovarian ***cancer*** in some studies. With only limited data, the assumption has been made that ***p53*** overexpression corresponds to ***p53*** mutations. The purpose of this investigation was to assess ***p53*** alterations in ovarian ***cancer*** to determine if ***p53*** overexpression corresponds with mutations in the ***p53*** gene, and to assess whether either predicts clinical outcome in ovarian ***carcinoma*** . Frozen ovarian ***carcinoma*** ***tumor*** specimens from 105 patients were analyzed by immunohistochemical staining for ***p53*** expression. SSCP was used to ***screen*** for mutations and DNA sequencing was used to confirm the specific ***mutation*** in exons 2 to 11, encompassing the entire ***p53*** open reading frame. Those ovarian carcinomas identified as wild-type ***p53*** by SSCP were subjected to automated DNA sequence analysis of the entire open reading frame. Relative to DNA sequence analysis, the sensitivity of SSCP was 85% and the specificity was 98%. Immunohistochemical staining demonstrated that 72 of the 105 (69%) cases had positive immunostaining. SSCP and DNA sequencing identified and confirmed mutations in 60 of the 105 carcinomas (57%). Although there was a statistically significant association between ***p53*** immunostaining and ***p53*** mutations (p = 0.0002), false-negative and -positive results were identified. ***Tumor*** grade (p = 0.03), ***stage*** (p = 0.08), and overall survival (p = 0.1 5) were moderately associated with positive ***p53*** immunostaining. Patients with ***p53*** mutations and overexpression had shorter overall patient survival (p = 0.02). The findings demonstrated that, individually, ***p53*** mutations and ***p53*** overexpression were each related to shorter patient survival, but the

strongest predictor of outcome was a combination of both mutations and overexpression. Comparisons of overall survival for women with mutations in loop 2, loop 3, and the loop-sheet-helix domains together showed a statistically significant difference in survival compared to survival of women whose ovarian cancers had other mutations (p = 0.046).

L17 ANSWER 6 OF 21 MEDLINE
ACCESSION NUMBER: 1999081511 MEDLINE
DOCUMENT NUMBER: 99081511
TITLE: PTEN ***mutation*** in endometrial cancers is associated with favorable clinical and pathologic characteristics.
AUTHOR: Risinger J I; Hayes K; Maxwell G L; Carney M E; Dodge R K; Barrett J C; Berchuck A
CORPORATE SOURCE: Laboratory of Molecular Carcinogenesis, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709, USA.
SOURCE: CLINICAL CANCER RESEARCH, (1998 Dec) 4 (12) 3005-10. Journal code: C2H. ISSN: 1078-0432.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY WEEK: 19990504
AB ***Mutation*** of the PTEN ***tumor*** suppressor gene is a frequent event in endometrial cancers. In other types of cancers, PTEN ***mutation*** has been associated with metastatic behavior and advanced ***stage*** . To examine the relationship between PTEN ***mutation*** and clinical features of endometrial cancers, we ***screened*** 136 cases for mutations in the nine exons and intronic splice sites of the PTEN gene, using single-strand conformation analysis, and aberrant bands were sequenced. Mutations were noted in 44 of 136 (32%) endometrial cancers, and two mutations were present in 8 cases. There were 36 cases with mutations resulting in truncated protein products, 6 cases with missense mutations in the phosphatase ***domain*** , 1 case with an in-frame deletion, and 1 case with a large insertion. ***Mutation*** of the PTEN gene correlated most closely with endometrioid histology; mutations were seen in only 5% (1 of 21) of serous/clear cell cancers compared with 37% (43 of 115) of endometrioid cancers (P = 0.004). PTEN ***mutation*** was associated with early ***stage*** , nonmetastatic disease and more favorable survival in both the entire group of 136 cases and in the 115 endometrioid cases. In addition, PTEN ***mutation*** correlated with other molecular features associated with favorable clinical behavior, including microsatellite instability and absence of ***p53*** overexpression. Microsatellite instability was found in 60% of cases with PTEN mutations compared with only 25% of cases without mutations (P = 0.004). Overexpression of ***p53*** was seen in only 14% of cases with PTEN mutations compared to 39% of cases without mutations (P = 0.006). In conclusion, PTEN ***mutation*** is associated with endometrioid histology and other favorable pathological, clinical, and molecular features rather than with increased metastatic potential as has been noted in some other types of cancers.

L17 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:767294 CAPLUS

DOCUMENT NUMBER: 130:166372
TITLE: MDM-2 oncoprotein overexpression, ***p53*** gene ***mutation*** , and VEGF up-regulation in angiosarcomas
AUTHOR(S): Zietz, Christian; Rossle, Matthias; Haas, Christian; Sendelhofert, Andrea; Hirschmann, Astrid; Sturzl, Michael; Lohrs, Udo
CORPORATE SOURCE: Department of Pathology, Ludwig Maximilians University of Munich, Munchen, 80337, Germany
SOURCE: Am. J. Pathol. (1998), 153(5), 1425-1433
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The endothelium is one of the largest cellular compartments of the human body and has a high proliferative potential. However, angiosarcomas are among the rarest malignancies. Despite this interesting contradiction, data on growth and angiogenesis control mechanisms of angiosarcomas are scarce. In this study of 19 angiosarcomas and 10 benign vascular control lesions we investigated the sequence and expression of the ***p53*** ***tumor*** suppressor gene and the expression of the mdm-2 proto-oncogene, which is a neg. regulator of ***p53*** activity and of the vascular endothelial growth factor (VEGF), whose expression, among other factors, is regulated by the ***p53*** /MDM-2 pathway. Ten sarcomas (53%) exhibited clear nuclear ***p53*** protein accumulation.

Two of these cases revealed mutations in the sequence-specific DNA binding ***domain*** of the ***p53*** gene. Thirteen angiosarcomas (68%) showed an increased amt. of MDM-2 protein. Elevated expression of ***p53*** and MDM-2 protein correlated with increased VEGF expression, which was found in nearly 80% of the angiosarcoma cases. Neg. or clearly lower immunostaining was obtained in cases from the benign control collective. Only one case of a juvenile hemangioma reached the cutoff value of ***p53*** positivity coincidentally with high VEGF expression. Our data suggest that the ***p53*** /MDM-2 pathway is impaired in about two-thirds (14/19) of the angiosarcomas. This may be a key event in the pathogenesis of human angiosarcomas. The increased VEGF expression obsd. supports this hypothesis.

REFERENCE COUNT: 46
REFERENCE(S):
(1) Beck, J; Hum Genet 1993, V91, P25 CAPLUS
(2) Beroud, C; Nucleic Acids Res 1996, V24, P147 CAPLUS
(3) Bornstein, P; Thrombospondins:Methods Enzymol 1994, V245, P62 CAPLUS
(9) Dameron, K; Cold Spring Harb Symp Quant Biol 1994, V59, P483 CAPLUS
(10) Dameron, K; Science 1994, V265, P1582 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 21 MEDLINE
ACCESSION NUMBER: 1998351428 MEDLINE
DOCUMENT NUMBER: 98351428
TITLE: ***p53*** mutations in cutaneous lesions induced in the hairless mouse by a solar ultraviolet light simulator.

AUTHOR: Queille S; Seite S; Tison S; Medaisko C; Drougard C; Fourtanier A; Sarasin A; Daya-Grosjean L
CORPORATE SOURCE: Laboratory of Molecular Genetics, Centre Nationale de Recherche Scientifique, Institut de Recherche sur le Cancer, Villejuif, France.
SOURCE: MOLECULAR CARCINOGENESIS, (1998 Jul) 22 (3) 167-74.
Journal code: AEQ. ISSN: 0899-1987.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981003

AB We investigated skin lesions induced in hairless SKH:HR1 mice by chronic exposure to a solar ultraviolet light (UV) simulator for alterations of the ***p53*** gene in ***conserved*** domains. Mutations of exons 5-8 of the ***p53*** gene in skin lesions were ***screened*** in 31 benign skin lesions (hyperplasias), 25 precancerous skin lesions (keratoacanthomas), and 25 malignant skin lesions (squamous cell carcinomas; SCC) by polymerase chain reaction-single-strand conformation polymorphism analysis. Most of the mutations occurred at dipyrimidine sequences located on the nontranscribed strand; the most frequent modifications were C-->T transitions (77%) and CC-->TT tandem mutations (5%); the latter are considered the UV fingerprint. ***p53*** mutations were detected in 3% of the hyperplasias, 12% of the keratoacanthomas, and 52% of the SCCs. Hence, the high frequency of ***p53*** mutations in SCCs compared with keratoacanthomas induced by a solar UV simulator suggested that, in our study, ***p53*** mutations probably occurred as a late event in the skin carcinogenesis progression of SCC. Interestingly, the level of CC-->TT tandem mutations in the SCCs (5%) was similar to that found in SCCs induced in hairless mice by UVB alone. ***p53*** protein was also detected in the different types of skin lesions by immunohistochemical analysis. Thus, our data from hairless mouse skin tumors induced by a solar UV simulator confirmed the major role of UVB-induced DNA damage in skin carcinogenesis and suggested that UVA plays a minor role in bringing about ***p53*** alterations.

L17 ANSWER 9 OF 21 MEDLINE
ACCESSION NUMBER: 1998001107 MEDLINE
DOCUMENT NUMBER: 98001107
TITLE: ***p53*** is a persistent and predictive marker in advanced ovarian carcinomas: multivariate analysis including comparison with Ki67 immunoreactivity.
AUTHOR: Rohlke P; Milde-Langosch K; Weyland C; Pichlmeier U; Jonat W; Loning T
CORPORATE SOURCE: Clinic of Gynecology and Obstetrics, University Hospital of Hamburg, Germany.
SOURCE: JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, (1997) 123 (9) 496-501.
Journal code: HL5. ISSN: 0171-5216.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104

AB ***p53*** ***mutation*** and ***p53*** protein overexpression are common findings in ovarian carcinomas. In order to evaluate the prognostic significance of the ***p53*** status and its role in metastasis, we examined 104 ovarian carcinomas, among them 83 cases with follow-up data, and 40 pairs of primary tumors and metastases, by ***p53*** immunohistochemistry and temperature-gradient gel electrophoresis. Comparison of primary tumors and their metastases revealed identical results in 88%-90% of the cases, indicating that, in most cases, mutant ***p53*** occurs prior to metastatic spread and remains clonally ***conserved*** . With respect to all tumors, moderate/high ***p53*** expression was significantly more prevalent in serous-papillary types, carcinomas with high grade, and high Ki67 scores, but was not associated with age, ***stage*** , or hormone receptor status. Kaplan-Meier analysis of 83 cases, followed-up for 9-96 months, demonstrated that moderate/high ***p53*** overexpression in the group of 66 ***stage*** T3/M1 tumors was associated significantly (P = 0.0028 and P = 0.0105) with shorter overall and recurrence-free survival. Multivariate analysis revealed that advanced clinical ***stage*** and ***p53*** positivity were the only independent predictive variables. No significance was seen in regard to second-look results and outcome of 50 patients receiving platinum-based chemotherapy. These observations show that p52 immunohistochemistry is an independent prognostic indicator at the given cut-off level, but does not reliably predict chemotherapy response.

L17 ANSWER 10 OF 21 MEDLINE
ACCESSION NUMBER: 97407358 MEDLINE
DOCUMENT NUMBER: 97407358
TITLE: ***p53*** gene mutations and expression of ***p53*** and mdm2 proteins in invasive breast ***carcinoma*** . A comparative analysis with clinico-pathological factors.
AUTHOR: Gunther T; Schneider-Stock R; Rys J; Niezabitowski A; Roessner A
CORPORATE SOURCE: Department of Pathology, Otto-von-Guericke University, Magdeburg, Germany.
SOURCE: JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, (1997) 123 (7).388-94.
Journal code: HL5. ISSN: 0171-5216.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971101
AB The aim of the study was to analyze ***p53*** gene mutations and the expression of ***p53*** and mdm2 proteins in 31 randomly selected invasive breast carcinomas. The results were then correlated with ***tumor*** grade, ***stage*** , estrogen receptor status, nodal status, and DNA ploidy. The expression of the proteins ***p53*** and mdm2 was determined immunohistochemically using formalin-fixed, paraffin-embedded material. ***Screening*** for ***p53*** ***mutation*** involved analysis of the highly ***conserved*** regions of the ***p53*** gene (exons 5-9) by the polymerase chain reaction/ single-strand conformation polymorphism (PCR-SSCP) technique. PCR products with band shifts were directly sequenced. Immunohistochemical staining of ***p53*** was positive in 9 cases (29.0%), only 2 of

which
showed a ***p53*** gene ***mutation*** . These were identified as
a
C-->G transversion at the second position of codon 278 in exon 8 and an
A-->G transition at the second position of codon 205 in exon 6. A third
case with a ***mutation*** was observed (C-->T transition, position 1
of codon 250 in exon 7) that did not show ***p53***
immunohistochemically. Of the 9 ***p53*** -positive tumors, 2 were
moderately differentiated (grade II). The remaining tumors were poorly
differentiated (7/9). By contrast, ***p53*** -negative carcinomas were
well differentiated (grade I) in most cases (P = 0.02). DNA cytometry in
8
of the 9 ***p53*** -positive carcinomas revealed an aneuploid stem
line. The majority of the ***p53*** -negative tumors were diploid (P =
0.01). Mdm2 oncoprotein was detected in 10 tumors (32.2%), 4 of which
were
p53 -positive, including the 3 with mutations. The grading of
the
mdm2-positive tumors was moderate or poor, G1 carcinomas were always
noted
to be mdm2-negative (P = 0.04). Overexpression of ***p53*** protein
is
a complex mechanism and does not merely indicate the detection of
mutations in the ***p53*** gene. This study has shown that
p53
expression correlates with ***tumor*** grade and DNA ploidy. Mdm2
expression was also associated with the ***tumor*** grade.
Immunohistological demonstration of the ***p53*** protein alone is
insufficient as a basis for comment on the functional state of the
p53 gene and gene product. The interrelation between
recognition
of the ***p53*** protein and gene ***mutation*** needs more
careful assessment to define their roles in the control of
neoplasia .

L17 ANSWER 11 OF 21 MEDLINE
ACCESSION NUMBER: 97057256 MEDLINE
DOCUMENT NUMBER: 97057256
TITLE: Provirus integration into a gene encoding a ubiquitin-conjugating enzyme results in a placental defect and embryonic lethality.
AUTHOR: Harbers K; Muller U; Grams A; Li E; Jaenisch R; Franz T
CORPORATE SOURCE: Heinrich-Pette-Institut fur Experimentelle Virologie und Immunologie, Universitat Hamburg, Germany.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Oct 29) 93 (22) 12412-7. Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
OTHER SOURCE: GENBANK-AF071557; GENBANK-X97042
ENTRY MONTH: 199702
AB Ubiquitin-conjugating enzymes (E2 or Ubc) constitute a family of
conserved proteins that play a key role in ubiquitin-dependent
degradation of proteins in eukaryotes. We describe here a transgenic
mouse
strain where retrovirus integration into an Ubc gene, designated UbcM4,
results in a recessive-lethal ***mutation*** . UbcM4 is the mouse
homologue of the previously described human UbcH7 that is involved in the

in vitro ubiquitination of several proteins including the ***tumor*** suppressor protein ***p53*** . The provirus is located in the first intron of the gene. When both alleles are mutated the level of steady-state mRNA is reduced by about 70%. About a third of homozygous mutant embryos die around day 11.5 of gestation. Embryos that survive that ***stage*** are growth retarded and die perinatally. The lethal phenotype is most likely caused by impairment of placenta ***development*** as this is the only organ that consistently showed pathological defects. The placental labyrinth is drastically reduced in size and vascularization is disturbed. The UbcM4 mouse mutant represents the first example in mammals of a ***mutation*** in a gene involved in ubiquitin conjugation. Its recessive-lethal phenotype demonstrates that the ubiquitin system plays an essential role during mouse ***development*** .

L17 ANSWER 12 OF 21 MEDLINE
ACCESSION NUMBER: 96184356 MEDLINE
DOCUMENT NUMBER: 96184356
TITLE: Molecular genetic differentiation between primary lung cancers and lung metastases of other tumors.
AUTHOR: Kandioler D; Dekan G; End A; Pasching E; Buchmayer H; Gnant M; Langmann F; Mannhalter C; Eckersberger F; Wolner E
CORPORATE SOURCE: Department of Surgery, University of Vienna Medical School, Austria.
SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1996 Apr) 111 (4) 827-31; discussion 832.
Journal code: K9J. ISSN: 0022-5223.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199608
AB When solitary pulmonary tumors are observed in patients with a history of ***cancer*** , differentiation between metastasis and primary lung ***cancer*** is crucial for appropriate therapy. Assuming that ***p53*** mutations are ***conserved*** in metastases, ***mutation*** analysis of the ***p53*** gene would be a valuable tool in differentiating metastases from primary carcinomas of the lung. In nine of 267 resected lung tumors, the origin of the lung ***tumor*** could not be defined histologically. Five patients had a history of colorectal ***carcinoma*** , one had a history of breast ***carcinoma*** , one had a history of soft-tissue ***carcinoma*** , and one had a history of head and neck ***carcinoma*** . One patient with a clear cell ***carcinoma*** of the lung had been surgically treated for both renal and thyroid ***cancer*** . Material from one patient with adenocarcinoma of the lung, histologically defined regional lymph nodes, and distant brain metastasis served as a control. We extracted deoxyribonucleic acid from the snap-frozen tissue of the unclassified lung tumors, from paraffin-embedded tissue of the previously removed primary cancers, and also from peripheral blood of the patients. Exons 2 to 11 of the ***p53*** gene were amplified in separated polymerase chain reactions and directly sequenced. In all cases, the presence of germline mutations was excluded by analysis of peripheral

blood deoxyribonucleic acid. The ***p53*** ***mutation*** detected in the deoxyribonucleic acid of the lung ***tumor*** of the control patient proved to be ***conserved*** in the lymph nodes as well as in the brain metastasis. In two cases, the lung tumors exhibited a ***p53*** ***mutation*** not present in the previously removed primary ***tumor*** and were therefore ***classified*** as new primary lung cancers. In five cases, the lung tumors proved to be metastases of the first ***tumor*** , exhibiting the identical ***p53*** ***mutation*** . One of these lung ***tumor*** samples could be identified as a metastasis from the renal ***cancer*** , but the corresponding thyroid ***cancer*** material was different. For two cases, molecular analysis remained inconclusive. In one case, no ***p53*** ***mutation*** could be found in the compared samples; in the other, no deoxyribonucleic acid could be extracted. Analysis of ***p53*** mutations allowed exact ***classification*** in tumors for which standard methods failed to distinguish between metastasis or primary ***tumor*** . More than two thirds of lung tumors in patients with previous gastrointestinal ***carcinoma*** were revealed to be metastases, but second primary lung ***cancer*** could also be ***diagnosed*** . This ***diagnosis*** allowed correct surgical and adjuvant treatment of these patients.

L17 ANSWER 13 OF 21 MEDLINE
ACCESSION NUMBER: 96181812 MEDLINE
DOCUMENT NUMBER: 96181812
TITLE: ***p53*** mutations in non-small cell lung carcinomas in Hong Kong.
AUTHOR: Lung M L; Wong M P; Skaanild M T; Fok C L; Lam W K; Yew W W
CORPORATE SOURCE: Department of Biology, Hong Kong University of Science and Technology, Kowloon.
SOURCE: CHEST, (1996 Mar) 109 (3) 718-26.
Journal code: D1C. ISSN: 0012-3692.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199608

AB Lung resections from 50 Chinese patients in Hong Kong ***diagnosed*** as having non-small cell lung ***carcinoma*** were examined for the presence of mutations in the ***p53*** gene by polymerase chain reaction single-stranded conformation polymorphism methods and for aberrant protein expression by immunostaining techniques. Eight-point mutations in the evolutionarily ***conserved*** exon 5 through 8 regions were detected. Abnormal expression of ***p53*** detectable by immunostaining techniques was seen in 23 specimens tested. There was no statistically significant correlation between the detection of ***p53*** aberrations and age, sex, smoking history, histologic type, and ***tumor*** ***stage*** . Aberrant ***p53*** protein levels detectable by immunostaining were significantly associated with the clinical and nodal staging of the tumors.

L17 ANSWER 14 OF 21 MEDLINE
ACCESSION NUMBER: 97092074 MEDLINE
DOCUMENT NUMBER: 97092074
TITLE: Hypothesis on a casual link between EMF and an evolutionary class of ***cancer*** and spontaneous abortion.
AUTHOR: Cooper W G
CORPORATE SOURCE: International Physics Health & Energy, Inc., Houston, Texas 77030, USA.
SOURCE: CANCER BIOCHEMISTRY BIOPHYSICS, (1996 Apr) 15 (3) 151-70. Ref: 57
Journal code: CL0. ISSN: 0305-7232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705

AB A biophysical theory is presented that supports a causal link between EMF exposures and the different biological endpoints of ***cancer*** and spontaneous abortion. The model for time-dependent instability of DNA specificity [Biochem. Genet. 32, 383 (1994)] is assumed to have been operational since DNA became selected as the molecular structure for the genome. Species were consequently required to adapt mechanisms to protect haploid gene pools from the continuous time-dependent accumulation of evolutionary base substitutions. To this end, ***conserved*** genetic domains containing ***mutation*** -intolerance thresholds are a result of natural selection operating on time-dependent base substitutions. " ***P53*** -type" genes are examples of such ***conserved*** domains with point ***mutation*** thresholds. When the oocyte is fertilized, ***conserved*** domains express wild type keto-amino genetic information. During subsequent ***development*** and growth, time-dependent evolution events populate G-C sites with enol-imine stationary states that can be transcribed and/or replicated to express transversion and transition mutations. As the level of evolution events would approach the intolerance threshold in the haploid genome, point ***mutation*** sensitive genes from ***conserved*** diploid domains, e.g. " ***p53*** -type" genes, would generate amino acid substituted proteins that have been evolutionarily selected to participate in species preservation by removing from the gene pool those haploid genomes containing advanced levels of ***mutation*** which, if propagated, would be inconsistent with survival. Consistent with the evolutionary origin of ***cancer*** hypothesis [***Cancer*** Biochem. Biophys: 13, 147 (1993)], perturbations that would enhance rates of populating G-C sites with enol-imine states could accelerate point ***mutation*** "activation" of " ***p53*** -type" genes that could be manifested as premature ***cancer*** in living populations or expressed as spontaneous abortion in unborn populations. The evolution event "rate constant" is (gamma/h)2 where gamma is the quantum mechanical energy shift between G-C states. This expression implies that "additional" magnetic fields could increase rates of populating enol-imine states due to Lorentz force momentum transfer to metastable proton oscillators where induced electric fields and local currents would subject elevated energy proton

oscillators to collisional de-exciatations which would increase the energy density of chemical bonds that support hydrogen bonds in DNA, thereby introducing larger energy shift values in (gamma/h)2. This hypothesis is explored for "additional" magnetic fields in the range of 0.15 to 0.01 gauss where the influence of magnetic enhancement energies on rates of populating enol-imine stationary states is evaluated, using Gurney and Condon tunneling time calculations for unperturbed and magnetically enhanced protons to escape metastable keto-amino energy wells. Model calculations are qualitative and are consistent with the experimentally testable hypothesis that "additional" magnetic fields could cause increased rates of accumulating evolutionary base substitutions, thereby increasing probabilities of activating " ***p53*** -type" genes which could cause increased incidence of spontaneous abortion in unborn populations and increased incidence of ***cancer*** in living populations.

L17 ANSWER 15 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95258956 EMBASE
DOCUMENT NUMBER: 1995258956
TITLE: New aspects of cell biology in osteosarcoma.
AUTHOR: Grundmann E.; Ueda Y.; Schneider-Stock R.; Roessner A.
CORPORATE SOURCE: Gerhard-Domagk-Institut Pathologie, Westfalische Wilhelms-Univ. Munster, Domagkstr 17.,D-48149 Munster, Germany
SOURCE: Pathology Research and Practice, (1995) 191/6 (563-570). ISSN: 0344-0338 CODEN: PARPDS
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Among the solid tumors of childhood and adolescence, osteosarcoma (OS) represents the most prominent example of efficient aggressive chemotherapy with secondary surgical therapy. A specific subclassification of the ***tumor*** is indispensable and must include recent results of cell biology. The co-distribution of different collagen types I-VI reflects the diverse differentiation of osteosarcoma cells, supporting the concept of a pluripotent mesenchymal cell to be the stem cell of the ***tumor*** . In contrast, osteonectin (SPARC) may not be considered as a reliable marker for osteosarcoma. The experience of special proteins being secreted by osteosarcoma cells is rather limited. Detailed molecular biological studies are still lacking. A loss of alleles on chromosome 27 particularly in the defined region 17p 13, can be observed in more than 75% of all OS, suggesting the contribution of a ***tumor*** suppressor gene, ***p53*** , located in that region. It is a 53 kd nucleophosphoprotein binding the major transforming protein, the large T antigen of Simian Virus 40. Immunohistological results showed positive staining with the antibody Pab 240 in 13 of 18 cases. In one osteoblastic OS, a novel splice ***mutation*** resulting in a fusing of exon 5 directly to exon 7 was detected. RB1 gene is also of major importance for the tumorigenesis of

OS. The multidrug resistance (mdr) is associated with a membrane-hound channel-forming transport protein, the P-glycoprotein. It is a ***conserved*** plasma membrane component of about 170 kd. Both the human isoforms mdr 1 and mdr 3 are localised in the long arm of chromosome
7. A statistically significant correlation between P-glycoprotein expression and response to chemotherapy for OS could not be, as of now fully established.

L17 ANSWER 16 OF 21 MEDLINE
ACCESSION NUMBER: 96128416 MEDLINE
DOCUMENT NUMBER: 96128416
TITLE: Molecular analysis of mutations in thyroid tumors with TGGE.
AUTHOR: Simon D; Goretzki P E; Schafer C; Gorelov V; Ebeling B; Roher H D
CORPORATE SOURCE: Department of Surgery, Heinrich Heine University Dusseldorf, Germany.
SOURCE: EXPERIMENTAL AND CLINICAL ENDOCRINOLOGY AND DIABETES, (1995) 103 (5) 275-9. Ref: 36
Journal code: CCV. ISSN: 0947-7349.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199604
AB Immunohistochemical demonstration of overexpression of the ***p53*** protein indicates a mutational alteration of the gene. Our own investigations of 59 differentiated thyroid carcinomas revealed an overexpression in 15% of the tumors. A correlation to unfavourable ***tumor*** prognosis was found (***stage*** I and II: 0/11 (0%); ***stage*** III: 4/26 (14%); ***stage*** IV: 5/22 (23%)). For ***screening*** of one out of more than 300 possible mutations temperature gradient gel electrophoresis was employed. Analysis of the highly- ***conserved*** regions of the ***p53*** gene (exon 5 to 8)
could demonstrate a ***mutation*** in only 1 out of 31 differentiated thyroid carcinomas. The question arises whether accumulation of the protein is due to a mutational event or rather other molecular mechanisms.

L17 ANSWER 17 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95147637 EMBASE
DOCUMENT NUMBER: 1995147637
TITLE: Overexpression of ***p53*** in hepatocellular carcinomas: A clinicopathological and prognostic correlation.
AUTHOR: Ng I.O.L.; Lai E.C.S.; Chan A.S.Y.; So M.K.P.
CORPORATE SOURCE: Department of Pathology, University of Hong Kong, Queen Mary Hospital, Pokfulam,Hong Kong, Hong Kong
SOURCE: Journal of Gastroenterology and Hepatology, (1995) 10/3 (250-255).
ISSN: 0815-9319 CODEN: JGHEEO
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
016 Cancer

048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Overexpression of the ***p53*** ***tumour*** suppressor gene is one of the most common abnormalities in primary human cancers and appears to be a result of point ***mutation*** within a highly ***conserved*** region of the gene with subsequent encoding for a mutant, more stable, protein. In this study, 71 surgically resected hepatocellular carcinomas (HCC) were examined to study the expression of the ***p53*** gene, its relation with clinicopathological parameters and its prognostic significance. Using immunohistochemical detection for mutant ***p53*** protein with monoclonal antibody PAb1801, ***p53*** overexpression was found in 22 tumours (31%) but in none of the non-tumorous liver specimens. Overexpression of ***p53*** was more frequent in tumours with poor cellular differentiation (P = 0.01), in tumours > 5 cm in diameter (P = 0.05), and in those with giant cells present (P = 0.03) and, less significantly, of massive type of Eggel's ***classification*** (P = 0.06). It did not have any significant correlation with hepatitis B or C status, background liver disease or serum .alpha.-fetoprotein levels, nor was it related to ***tumour*** invasiveness (venous permeation, direct liver invasion and ***tumour*** microsatellite formation). In addition, the presence of ***p53*** mutant protein did not influence ***tumour*** recurrence or patients' survival rates. The data suggested that ***p53*** ***mutation*** in HCC was associated with a later ***stage*** of oncogenesis. However, it was not apparently related to ***tumour*** invasiveness/aggressiveness and prognosis.

L17 ANSWER 18 OF 21 MEDLINE
ACCESSION NUMBER: 95384986 MEDLINE
DOCUMENT NUMBER: 95384986
TITLE: Lack of ***p53*** point mutations in chemically induced mouse hepatoblastomas: an end- ***stage*** , highly malignant hepatocellular ***tumor*** .
AUTHOR: Calvert R J; Tashiro Y; Buzard G S; Diwan B A; Weghorst C M
CORPORATE SOURCE: Office of Special Nutritionals, United States Food and Drug Administration, Laurel, MD, USA..
SOURCE: CANCER LETTERS, (1995 Aug 16) 95 (1-2) 175-80. Journal code: CMX. ISSN: 0304-3835.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199512
AB Inactivation of the ***p53*** ***tumor*** suppressor gene appears to be an important event in the progression of many types of human ***neoplasms*** ; however its role in rodent experimental tumorigenesis is controversial. Previous studies have shown that a wide array of chemically induced and spontaneous mouse liver tumors lack ***p53*** mutations within the evolutionarily ***conserved*** regions of exons 5-8. However, since ***p53*** inactivation in human ***neoplasms*** occurs relatively late in ***tumor*** progression, it is possible that the mouse liver tumors evaluated previously were not suitably advanced to incur ***p53*** aberrations. In the present study, we examined an

end-
stage , highly malignant embryonal mouse liver ***tumor*** known as the hepatoblastoma (HB) for ***p53*** mutations utilizing the highly sensitive 'cold' single-strand conformation polymorphism (SSCP) technique. In addition, several of the HBs were examined by direct nucleotide sequencing. No aberrations of the ***p53*** gene were detected within exons 5-8 of any of the 16 HBs examined. These results confirm that the ***p53*** gene plays a minimal role in the ***development*** or malignant progression of hepatocellular tumors in mice.

L17 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:6171 CAPLUS
DOCUMENT NUMBER: 120:6171
TITLE: Timing of ***p53*** mutations during astrocytoma tumorigenesis
AUTHOR(S): del Arco, Araceli; Garcia, Juan; Arribas, Carmen; Barrio, Rosa; Blazquez, Martin G.; Izquierdo, Jose M.; Izquierdo, Marta
CORPORATE SOURCE: Fac. Cienc., Univ. Auton. Madrid, Madrid, 28049, Spain
SOURCE: Hum. Mol. Genet. (1993), 2(10), 1687-90
CODEN: HMGEE5; ISSN: 0964-6906
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a combination of polymerase chain reaction. and single-strand conformation polymorphism techniques (PCR-SSCP) the authors have analyzed 78 brain ***tumor*** samples (80 primary and 8 metastatic) for the presence of mutations in the ***conserved*** regions of the Tp53 (***tumor*** ***p53***) gene. The authors have found that only two groups, gliomas (exclusively in astrocytomas) and metastases, displayed Tp53 mutations. Three of eight (37.5%) metastases showed a mutant Tp53 allele accompanied by loss of the normal one. In contrast, the frequency of Tp53 mutations in the primary brain tumors examd. was lower (5.7%). Although the authors have examd. different types of primary brain tumors, Tp53 mutations were exclusively obsd. in both, low and high-grade astrocytomas (four of 24). The Tp53 mutations detected in astrocytic tumors appear to be correlated with the malignancy grade. The low-grade astrocytomas were heterozygous for the ***mutation*** , whereas the high-grade astrocytomas had affected the two Tp53 alleles, suggesting a two-steps model for inactivation of the ***p53*** gene in astrocytomas. Thus, single ***p53*** ***mutation*** seems to occur in initial stages of astrocytoma tumorigenesis; the later lost of the remaining wild-type allele appears assocd. with the progression towards a more malignant ***stage*** .

L17 ANSWER 20 OF 21 MEDLINE
ACCESSION NUMBER: 92315228 MEDLINE
DOCUMENT NUMBER: 92315228
TITLE: ***p53*** mutations in C57BL/6J murine thymic lymphomas induced by gamma-irradiation and N-methylnitrosourea.
AUTHOR: Brathwaite O; Bayona W; Newcomb E W
CORPORATE SOURCE: New York University, New York..
CONTRACT NUMBER: CA 40533 (NCI)
SOURCE: CANCER RESEARCH, (1992 Jul 1) 52 (13) 3791-5.

Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199210
AB Genomic DNA from thymus tissue obtained from 47 C57BL/6J animals treated with the DNA alkylating agent N-methylnitrosourea or gamma-irradiation were ***screened*** for the presence of ***p53*** mutations by using the single strand conformation polymorphism assay. Mutations were detected in 13% (4 of 30) of primary thymic lymphomas but none of 17 early ***stage*** lymphomas. The frequency of ***p53*** mutations was the same in tumors induced by N-methylnitrosourea (2 of 15) or by gamma-irradiation (2 of 15). Mutations occurred in the highly ***conserved*** regions of the ***p53*** gene in exons 5, 7, and 8. G:C to A:T transitions were commonly observed. One of 4 of the tumors analyzed contained two ***p53*** mutations in exons 7 and 8. A previous study of the same tumors showed that ras mutations occurred with high frequency (greater than 50%) (E. W. Newcomb et al., ***Cancer*** Res., 48:5514-5521, 1988). Our data suggest that ***p53*** mutations do not play a major role in carcinogen-induced thymic lymphomas studied here.

L17 ANSWER 21 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92153562 EMBASE
DOCUMENT NUMBER: 1992153562
TITLE: Overexpression and ***mutation*** of ***p53*** in endometrial ***carcinoma*** .
AUTHOR: Kohler M.F.; Berchuck A.; Davidoff A.M.; Humphrey P.A.; Dodge R.K.; Iglehart J.D.; Soper J.T.; Clarke-Pearson D.L.; Bast Jr. R.C.; Marks J.R.
CORPORATE SOURCE: Duke University Medical Center, Box 3079,Durham, NC 27710, United States
SOURCE: Cancer Research, (1992) 52/6 (1622-1627).
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Immunohistochemical staining for the ***p53*** protein was performed in 107 snap frozen primary endometrial adenocarcinomas and 15 benign uterine tissues using monoclonal antibody PAb1801. No staining was seen in benign samples, whereas intense nuclear staining of ***cancer*** cells consistent with overexpression of the ***p53*** protein was observed in 22 of 107 cancers (21%). ***p53*** overexpression was more frequent in advanced (***Stage*** III/IV) cancers (41%) than in early (***Stage*** I/II) cancers (9%) (P < 0.001), and also was associated with nonendometrioid histology (P = 0.008), positive peritoneal cytology (P = 0.01), extrauterine metastases (P = 0.003), and negative progesterone

receptor status (P = 0.04). To confirm the relationship between ***p53*** overexpression and ***mutation*** , ***p53*** mRNA from 8 cancers was reverse transcribed and amplified using the polymerase chain reaction. DNA sequencing revealed point mutations in each of the 5 cancers that overexpressed ***p53*** , whereas the wild-type sequence was found in 3 cancers that did not overexpress the protein. Each of the 5 mutations resulted in an amino acid substitution in a highly ***conserved*** region of the ***p53*** gene where mutations have been found in other cancers. Further studies are warranted to determine whether the association between ***p53*** overexpression and advanced ***stage*** disease is due to accumulation of genetic lesions during ***tumor*** progression or whether ***p53*** alterations confer a more virulent phenotype.